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Fredrik Nilsson

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EXAMINER

STEELE, AMBER D

ART UNIT

PAPER NUMBER

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/798,097	<b>Applicant(s)</b> NILSSON, FREDRIK	
	<b>Examiner</b> AMBER D. STEELE	<b>Art Unit</b> 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on May 19, 2009 and June 10, 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-21, 24, 26 and 27 is/are pending in the application.
- 4a) Of the above claim(s) 12, 15, 16, 19 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13, 14, 17, 18, 21, 24, 26 and 27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2009 has been entered.

### ***Status of the Claims***

2. Claims 38-39, 44, and 47 were canceled in the amendment to the claims received on February 15, 2006.

Claims 22-23, 28-37, 40-43, 45-46, and 48-49 were canceled and claims 1-2, 7, 9, 10, 14, 21, and 24-27 were amended in the amendment to the claims received on August 25, 2006.

The amendment to the claims received on November 19, 2007 amended claim 1.

The amendment to the claims received on August 20, 2008 amended claims 1-6, 8, 14, and 26-27 and canceled claim 25.

The amendment to the claims received on February 19, 2009 changed the status identifiers only.

The amendment to the claims received on June 10, 2009 amended claim 1.

Claims 1-21, 24, and 26-27 are currently pending.

Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are currently under consideration.

***Election/Restrictions***

3. Applicant elected, with traverse, antibody as the species of binding molecule, C-terminal motif as the species of motif, and at least 10% as the species of capture in the reply filed on February 15, 2006. Claims 12, 15-16, and 19-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected species, there being no allowable generic or linking claim.

***Priority***

4. The present application claims priority to U.S. provisional application 60/454,229 filed March 12, 2003.

***Invention as Claimed***

5. A method for analyzing a heterogeneous sample comprising a mixture of proteins, peptides, protein fragments, or peptide fragments wherein the composition of the heterogeneous sample is unknown prior to conducting the method, the method comprising (a) separating the heterogeneous sample of proteins, peptides, or protein fragments, or peptide fragments, into heterogeneous classes by binding members of each class to a spaced apart defined location on an array, wherein more than one protein, peptide, protein fragment, or peptide fragment binds to each defined location on the array, and wherein members of each class have a motif common to that class; and (b) characterizing the proteins, peptides, protein fragments, or peptide fragments, in each class by determining the mass of the proteins, peptides, protein fragments, or peptide fragments in the heterogeneous classes, and determining the abundance of proteins, peptides, protein fragments, or peptide fragments, of different mass in the heterogeneous classes and variations thereof.

### **New Objections**

6. Claim 1 is objected to because of the following informalities: in line 3, heterogeneous is misspelled. Appropriate correction is required.

### **New Rejection**

#### ***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-11, 13, 14, 17, 18, 21, 24, 26, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Applicants have neglected to point out support in the originally filed specification for the claim amendments received on June 10, 2009. While “mixture” was found in the originally filed specification, “unknown” was not.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-11, 13, 14, 17, 18, 21, 24, 26, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to

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determine the scope of the presently claimed invention. The term "unknown" in present independent claim 1 is a relative term which renders the claim indefinite. The term "unknown" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The recitation of "wherein the composition of the heterogeneous sample is unknown prior to conducting the method" renders the instant claims indefinite and the claim language can be interpreted in various manners. The instant specification does not specifically define the term "unknown" to be of any time frame or to any particular entity. Further, it is not clear if the sample is "unknown" at the time of filing of the instant application or at any other time. It is also not clear if the samples are "unknown" by a specific entity, all entities, etc. That is a sample might be "unknown" to one experimenter, but may not be "unknown" by another experimenter. Thus, one of ordinary skill in the art would not recognize the metes and bounds of the instant claimed invention.

### **Maintained Rejections**

#### ***Claim Rejections – 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002) and Nelson et al. U.S. Patent 6,887,713 (effective filing date of March 11, 2000).

For present claim 1, Minden et al. teach methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden et al. teach that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized (please refer to paragraphs [0003-0004], [0030], [0036], [0048]; Figures 7-9). Furthermore, Minden et al. teach that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location (please refer to Figures 4A-4C and 5 and paragraphs 89-96).

For present claim 2, Minden et al. teach that the total protein content of a cell or tissue can be utilized as the protein mixture (please refer to paragraphs [0035], [0066]).

For present claims 3-6, Minden et al. teach that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin (please refer to paragraph [0037-0039], [0066], [00105], [00107], and Table 1).

For present claims 7-8 and 11, Minden et al. teach that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues (please refer to Table 1 and paragraphs [0041-0045], [0049], [0054], [0063]).

For present claims 9-10, Minden et al. teach that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids (please refer to paragraphs [0029], [0032], [0040-0046], [0054], [00113-00116]).

For present claim 13, Minden et al. teach that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents (please refer to paragraphs [0005], [0008], [0012], [0028], [0040]).

For present claim 14, Minden et al. teach that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture (please refer to paragraph [0035], [0040]).

For present claim 17, Minden et al. teach that the array can have 2-100 different proteins (please refer to paragraphs [0047], [0073-0074]).

For present claim 18, Minden et al. teach that the binding reagents can be antibodies (please refer to paragraphs [0029], [0056-0061], [0072]).

For present claim 21, Minden et al. teach that the proteins are compared to a reference set (i.e. characterizing; please refer to paragraphs [0005], [0028-0031], [0040]).

For present claim 27, Minden et al. teach that various binding reagents can be compared to a reference set or to other binding reagents (please refer to paragraphs [0005], [0030-0031], [0040], [0053]).

However, Minden et al. does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry.

For present claims 1, 24, and 26, Nelson et al. teach analyzing complex biological mixtures utilizing “lab-on-a-chip” (i.e. chip-based microarrays) and MALDI-TOF (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry) wherein the proteins are quantified (i.e. abundance), internal reference standards

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are utilized, and determining the amount (i.e. abundance) of the proteins (please refer to the entire specification particularly the abstract; Figures 1, 4, 7, 8a-c, and 10a-c; column 1, lines 54-67; columns 2-3; column 4, lines 1-30; column 6, lines 52-67; column 8, lines 19-64; column 9, lines 13-35; columns 10-11 and 14-15; column 16, lines 1-10; column 17, lines 30-45).

The claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only as taught by Minden et al.) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF as taught by Nelson et al.) would have yielded predictable results (i.e. analysis of both mass and abundance at the same time) to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

Therefore, the teaching of Minden et al. and Nelson et al. render the presently claimed invention *prima facie* obvious.

### ***Arguments and Response***

13. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Minden et al. and Nelson et al. for claims 1-11, 13-14, 17-18, 21, 24, and 26-27 were considered but are not persuasive for the following reasons.

Applicants contend that the present invention is drawn to a method utilizing protein/peptide mixtures and unknown samples.

Applicants' arguments are not convincing since the teachings of Minden et al. and Nelson et al. render the method of the instant claims *prima facie* obvious. All previous arguments of record are incorporated by reference.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's arguments, the recitation "mixture" and "wherein the composition of the heterogeneous sample is unknown prior to conducting the method" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In addition, both Minden et al. and Nelson et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both homogenous and heterogeneous methods). See Minden et al. paragraphs 3-4 and 136 and Nelson et al. columns 9-10. Furthermore, Minden et al. teach heterogeneous protein mixtures including proteolytic cleavage of proteins (please refer to paragraphs 29-35). Moreover, Minden et al. teach that the protein mixture can be all of the proteins in a given organism, proteome, organ, tissue, cell, organelle, or sub-cellular localization (see paragraph 35) and thus all of the proteins are not

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necessarily known. Nelson et al. teach utilizing MALDI-TOF for quantitative analysis including analysis of proteins from biofluids, heterogeneous analyte systems, sample comprising point mutations, etc. (i.e. heterogeneous sample; see column 2, lines 42-46; paragraph spanning columns 3-4; columns 5, 8-11, 15-16; Examples 3 and 6).

“The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain.” *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). See MPEP § 2123. In addition, paragraph 35 of Minden et al. defines “protein mixture” and paragraph 66 teaches that “trypsin-digested yeast total protein is affixed to a surface...and binding reagent-displaying phage are absorbed on the surface...[d]igested total protein from any given protein mixture may be used...”. Therefore, while the specific example in paragraph 66 refers to having the protein mixture on the array, one of skill in the art could envision either phage displaying the trypsin-digested yeast total protein or utilizing the phage displayed peptides on the support and adding in the protein mixture since the end result (e.g. screening for specific binding between the two groups of molecules) would be the same. The claims would have been obvious because the substitution of one known element (i.e. protein mixture on a support, adding binding molecules to support comprising protein mixture taught by Minden et al.) for another (i.e. protein mixture free from support, added to support comprising binding molecules) would have yielded predictable results (i.e. screening for binding) to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. binding molecules on support or

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free in solution and added to support to screen for binding) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

In addition, both arrays and polyclonal antibodies are well-known in the art. Furthermore, the presently claimed invention is not currently drawn to a method of using a polyclonal antibody array. It is also noted that the presently claimed invention states that the molecules on the array “is capable of binding specifically to a motif” (see present claim 13) and “the motif being constant between all peptides, or protein, or peptide fragments” (see present claim 10). Therefore, each discrete location on the array binds to the same motif. While the individual proteins or peptides in the heterogeneous sample may be different, each spot on the array binds to the same motif (i.e. the presently claimed invention is drawn to “mono-specific binding reagents” at each spot on the array wherein different spots comprise different binding reagents which is typical of arrays described in the prior art).

14. Claims 1-11, 13-14, 17-18, 21, 24, and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002) and Barry et al. WO 02/25287 (filed September 19, 2001).

For present claim 1, Minden et al. teach methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden et al. teach that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized (please refer to

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paragraphs [0003-0004], [0030], [0036], [0048]; Figures 7-9). Furthermore, Minden et al. teach that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location (please refer to Figures 4A-4C and 5 and paragraphs 89-96).

For present claim 2, Minden et al. teach that the total protein content of a cell or tissue can be utilized as the protein mixture (please refer to paragraphs [0035], [0066]).

For present claims 3-6, Minden et al. teach that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin (please refer to paragraph [0037-0039], [0066], [00105], [00107], and Table 1).

For present claims 7-8 and 11, Minden et al. teach that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues (please refer to Table 1 and paragraphs [0041-0045], [0049], [0054], [0063]).

For present claims 9-10, Minden et al. teach that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids (please refer to paragraphs [0029], [0032], [0040-0046], [0054], [00113-00116]).

For present claim 13, Minden et al. teach that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents (please refer to paragraphs [0005], [0008], [0012], [0028], [0040]).

For present claim 14, Minden et al. teach that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture (please refer to paragraph [0035], [0040]).

For present claim 17, Minden et al. teach that the array can have 2-100 different proteins (please refer to paragraphs [0047], [0073-0074]).

For present claim 18, Minden et al. teach that the binding reagents can be antibodies (please refer to paragraphs [0029], [0056-0061], [0072]).

For present claim 21, Minden et al. teach that the proteins are compared to a reference set (i.e. characterizing; please refer to paragraphs [0005], [0028-0031], [0040]).

For present claim 27, Minden et al. teach that various binding reagents can be compared to a reference set or to other binding reagents (please refer to paragraphs [0005], [0030-0031], [0040], [0053]).

However, Minden et al. does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry.

Barry et al. teach methods of determining the binding and mass of trypsin digested proteins including antibodies from a cell including phage or tissue sample immobilized on an array (please refer to the abstract, pages 2-6, 21-30, Figures 3-6 and 8-10, Examples 2-3).

For present claim 1, Barry et al. teach determining the abundance of proteins via MALDI-TOF (i.e. mass; please refer to pages 5-6, page 32, lines 25-33, page 33, lines 21-37, pages 34-35, Figures 3-6 and 8-10, Examples 2-3).

For present claim 24, Barry et al. teach MALDI-TOF (i.e. matrix assisted laser desorption ionization-time of flight) mass spectrometry (i.e. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry or CID; page 35, line 7;

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please refer to pages 5-6, page 32, lines 25-33, page 33, lines 21-37, pages 34-35, Figures 3-6 and 8-10, Examples 2-3).

For present claim 26, Barry et al. teach determining the abundance of the protein via MALDI-TOF including proteins from any given starting material (i.e. unfragmented parent protein; please refer to page 3, lines 28-30; pages 5-6; page 32, lines 25-33; page 33, lines 21-37; pages 34-35; Figures 3-6 and 8-10, Examples 2-3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of identifying proteins taught by Minden et al. with the MALDI-TOF analysis taught by Barry et al.

One having ordinary skill in the art would have been motivated to do this because Barry et al. teach that the use of mass spectrometry and MALDI-TOF provide semi-quantitative and quantitative results for protein microarrays (please refer to page 1, lines 20-26 and 34-37; page 2, lines 1-24; page 3, lines 5-30; Examples 2-3).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of identifying proteins taught by Minden et al. with the MALDI-TOF analysis taught by Barry et al. because of the examples provided by Barry et al. show that trypsin digested antibody arrays can be quantitated via MALDI-TOF (please refer to Examples 2-3).

Therefore, the modification of the method of identifying proteins taught by Minden et al. with the MALDI-TOF analysis taught by Barry et al. render the instant claims *prima facie* obvious.

***Arguments and Response***

15. Applicant's argument directed to the rejection under 35 USC 103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002) and Barry et al. WO 0225287 (filed September 19, 2001) for claims 1-11, 13-14, 17-18, 21, 24, and 26-27 was considered but was not persuasive for the following reasons.

Applicants contend that the present invention is drawn to a method utilizing protein/peptide mixtures and unknown samples.

Applicant's argument is not convincing since the combined teachings of Minden et al. and Barry et al. do render the method of the instant claims *prima facie* obvious. All previous arguments of record are incorporated by reference.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's arguments, the recitation "mixture" and "wherein the composition of the heterogeneous sample is unknown prior to conducting the method" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

In addition, both Minden et al. and Barry et al. discuss utilizing mass spectrometry in methods of identifying proteins (i.e. utilizing mass spectrometry in both homogenous and heterogeneous methods). See Minden et al. paragraphs 3-4 and 136 and Barry et al. pages 33-35. Furthermore, Minden et al. teach heterogeneous protein mixtures including proteolytic cleavage of proteins (please refer to paragraphs 29-35). Moreover, Minden et al. teach that the protein mixture can be all of the proteins in a given organism, proteome, organ, tissue, cell, organelle, or sub-cellular localization (see paragraph 35) and thus all of the proteins are not necessarily known. Barry et al. teach quantitative or semi-quantitative analysis via MALDI-TOF wherein the sample can include body fluid, tissue, or cell (i.e. heterogeneous; please refer to pages 3, 9, 21, 28, 32-34, 45-46).

“The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain.” *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). See MPEP § 2123. In addition, paragraph 35 of Minden et al. defines “protein mixture” and paragraph 66 teaches that “trypsin-digested yeast total protein is affixed to a surface...and binding reagent-displaying phage are absorbed on the surface...[d]igested total protein from any given protein mixture may be used...”. Therefore, while the specific example in paragraph 66 refers to having the protein mixture on the array, one of skill in the art could envision either phage displaying the trypsin-digested yeast total protein or utilizing the phage displayed peptides on the support and adding in the protein mixture since the end result (e.g. screening for specific binding between the two groups of molecules) would be

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the same. The claims would have been obvious because the substitution of one known element (i.e. protein mixture on a support, adding binding molecules to support comprising protein mixture taught by Minden et al.) for another (i.e. protein mixture free from support, added to support comprising binding molecules) would have yielded predictable results (i.e. screening for binding) to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. binding molecules on support or free in solution and added to support to screen for binding) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

In addition, both arrays and polyclonal antibodies are well-known in the art. Furthermore, the presently claimed invention is not currently drawn to a method of using a polyclonal antibody array. It is also noted that the presently claimed invention states that a molecule on the array “is capable of binding specifically to a motif” (see present claim 13) and “the motif being constant between all peptides, or protein, or peptide fragments” (see present claim 10). Therefore, each discrete location on the array binds to the same motif. While the individual proteins or peptides in the heterogeneous sample may be different, each spot on the array binds to the same motif (i.e. the presently claimed invention is drawn to “mono-specific binding reagents” at each spot on the array wherein different spots comprise different binding reagents which is typical of arrays described in the prior art).

***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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